EDITORIALS

Surfactant Protein-B in Chronic Heart Failure: An Insight to the Alveolocapillary Barrier

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Chronic heart failure (CHF) is acknowledged as a modern and growing epidemic with an enormous social and economic burden. Given that the cardinal clinical manifestation of CHF is dyspnea, it is remarkable that respiratory abnormalities in this complex clinical syndrome are so seldom the focus of attention by the cardiovascular research fraternity. A pulmonary based focus on CHF may yield important pathophysiologic information and pave the way for advances in the management of this common and complex condition. In their paper in this issue of Revista Española de Cardiología Pascual-Figal et al1 take a step in this direction by confirming an increase in circulating surfactant protein-B (SP-B) in CHF and noting for the first time a relationship with ventilatory inefficiency.2

The alveolocapillary barrier separates alveolar gas from pulmonary blood. It is by necessity extremely thin and has a large surface area to allow sufficient and speedy gas diffusion. The alveolar epithelial cells form the external layer and the endothelial cells the internal layer. Both cell layers are supported by their respective basement membranes. Between the epithelial and endothelial basement membranes is the pulmonary interstitial space. This is only a potential space in the gas exchange regions. Type I alveolar epithelial cells are large, extremely flattened cells which cover 95% of the lung’s surface area. These cells form a thin lining over the external interface (alveolar surface) and bind to adjacent cells via tight intercellular junctions. The type II alveolar epithelial cell is the more complex alveolar epithelial cell. It is a cuboidal highly metabolically active cell whose best-appreciated function is the synthesis and secretion of pulmonary surfactant. The pulmonary endothelial cells line the capillaries within the lung parenchyma (Figure).

Exposure of the fragile alveolocapillary barrier to raised pulmonary microvascular pressure as a consequence of heart failure (both acute and chronic) and the exposure of the components of the barrier to the hormonal and cytokine milieu of heart failure has multiple incompletely explored effects on its structure and function. These range from protein pore stretching to stress failure3 and inflammatory damage4 to fibrosis.

SP-B is one of the 4 surfactant specific proteins. It is a quantitatively minor but physiologically critical component of pulmonary surfactant.5,6 It is produced by the type II alveolar epithelial cell and has no other known or suspected side of synthesis.6 Since there is a large concentration gradient of SP-B from the alveolar surfactant layer across the alveolocapillary barrier to the circulation where it is rapidly cleared, circulating levels are increased in conditions of alveolocapillary barrier damage.6,7

The term pneumoproteinaemia has been coined to describe the abnormal presence of lung specific proteins (such as SP-B) in the circulation and their ability to reflect lung disorders by reflecting the health of the alveolocapillary barrier.8 Circulating SP-B has been found to be elevated in acute respiratory distress syndrome,9 acute cardiogenic pulmonary oedema10 and chronic heart failure.11 This SP-B work was performed using a competitive ELISA.

In their study Pascual-Figal et al have demonstrated an increase in circulating SP-B in CHF patients compared to healthy volunteers.2 This is a noteworthy observation for 2 reasons. Firstly, it confirms the only other report of increased SP-B in CHF11 and secondly it does so using a different measurement technique in a different laboratory (Western Blot). Given the known changes in the structure and function of the alveolocapillary barrier in CHF this observation might not have been expected. Like in mitral stenosis the chronic exposure of the fragile alveolocapillary barrier to high pulmonary microvascular pressure in CHF results in adaptive structural changes in order to...
At a clinical level it has only been relatively recently acknowledged that a significant part of the reduction in exercise performance in CHF reflects reduced gas exchange. This physiological abnormality is reflected in the reduction in peak oxygen consumption (VO$_2$) and the increase in the slope of the linear relationship between ventilation (VE) and the production of carbon dioxide (VCO$_2$); VE/VCO$_2$ slope. These 2 physiologic variables are prognostically important in CHF. It follows that a relationship between a circulating biomarker which reflects the health of the alveolocapillary barrier (SP-B) and cardio-respiratory variables which reflects the function of the alveolocapillary barrier (VO$_{2\text{max}}$ and VE/VCO$_2$ slope) would be of interest both clinically and from a pathophysiologic viewpoint. Pascual-Figal et al have for the first time demonstrated that ventilatory inefficiency as measured by the VE/VCO$_2$ slope is related to circulating SP-B levels thereby linking these 2 markers of abnormal alveolocapillary barrier function in CHF. They point out that the relationship between brain natriuretic peptide levels and VO$_{2\text{max}}$ is intuitive given their close relationship to cardiac output while the SP-B and the VE/VCO$_2$ slope relationship reflects a different fundamental abnormality in CHF; the state of the alveolocapillary barrier.

Much work is still required at both the basic science and clinical science level in exploring the respiratory consequences of CHF. It is a fertile field of potential research as it tends to lie between cardiac researchers who focus on the heart and vasculature in CHF and pulmonary researchers who tend to focus on the lungs in what are traditionally considered “pulmonary diseases,” which CHF is not. The observations of Pascual-Figal et al remind us that in the complex clinical syndrome of CHF there are pulmonary consequences of cardiac disease.

REFERENCES